Using Gnuplot for Model Fitting

Biochemistry Boot Camp
Session #4
Nick Fitzkee
nfitzkee@chemistry.msstate.edu

Think and Discuss

What is a scientific model?

Properties of Models

- Explain an observable quantity (e.g. measured heat, growth rate, etc.)
- Express quantity in terms of understandable parameters and fundamental constants (equilibrium constant, rate constants, etc.)
- Should be predictive (so we can test the model)

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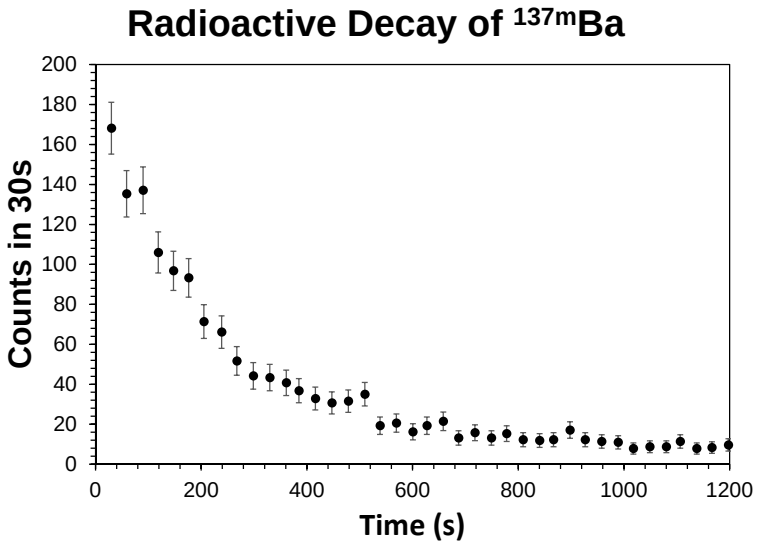
Example Radioactive Decay



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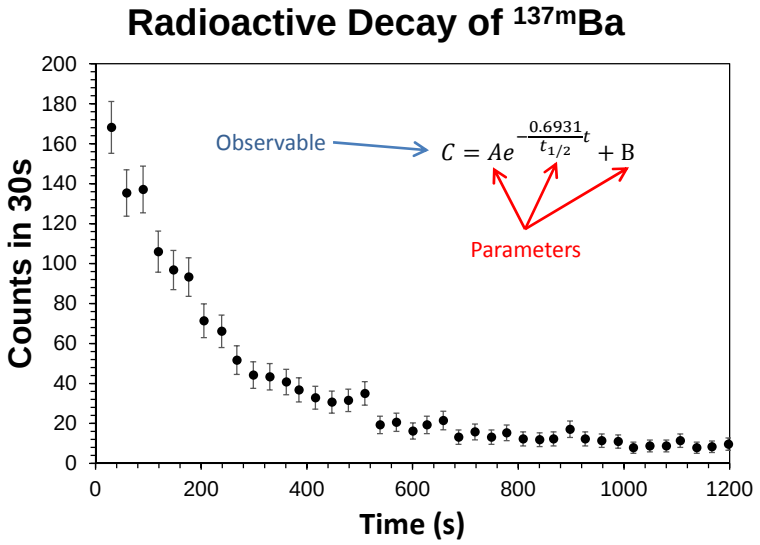
Example Radioactive Decay



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How to Find Parameters?

- Minimize the difference between the observed and model-calculated values:

$$\chi_n^2 = \frac{1}{N_d}\sum_i \left\{\frac{1}{\sigma_i^2}[y_i - f(x_i)]^2\right\}$$

- Definitions:
  - y_i = observed data point i
  - $f(x_i)$ = model calculated point x_i (will change when parameters are changed)
  - σ_i = uncertainty for point i
  - N_d = # of observations - # of parameters

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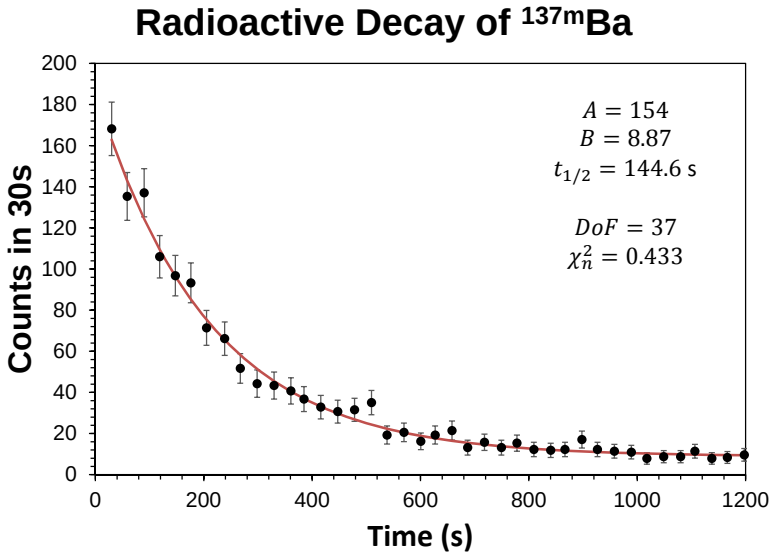
Example Radioactive Decay



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Think and Discuss

The accepted half-life for ^{137m}Ba is 153 s. Is our value of 144.6 good?

Examples: Biochemical Models

- Single site binding: $P + L \rightleftarrows PL$

$$\bar{\nu} = \frac{[PL]}{P_0} = \frac{(P_0 + L_0 + K) - \sqrt{(P_0 + L_0 + K)^2 - 4P_0L_0}}{2P_0}$$

- Folding vs. Temperature: $\mathrm{N} \rightleftarrows U$

$$f = \frac{1}{1+K} = \frac{1}{1 + e^{-(\Delta\bar{H}^0 - T\Delta\bar{S}^0)/RT}}$$

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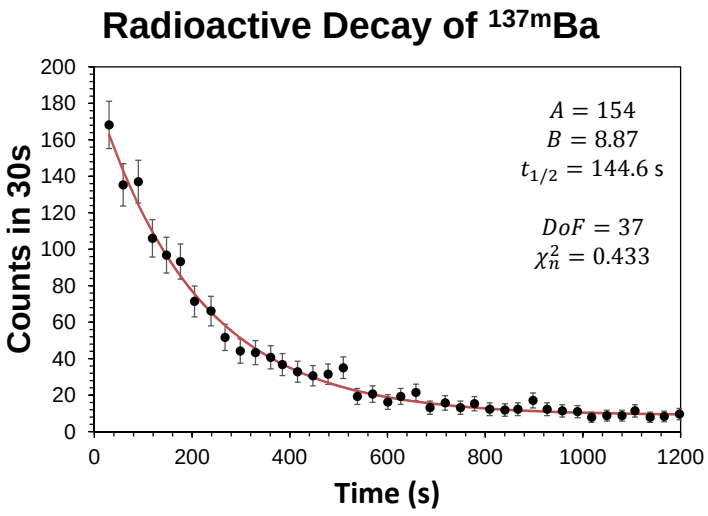
How to Assess a Fit:

#1: Does the fit look good?



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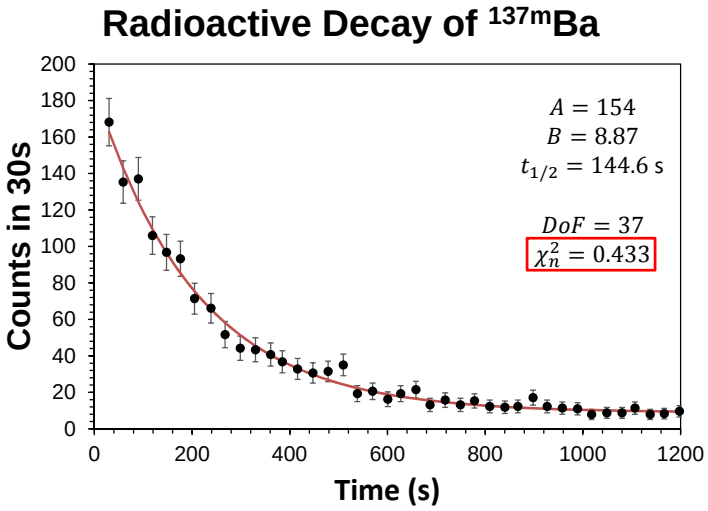
How to Assess a Fit:

#2: Is Normalized Chi-Square (χ_n^2) ≤ 1.0?



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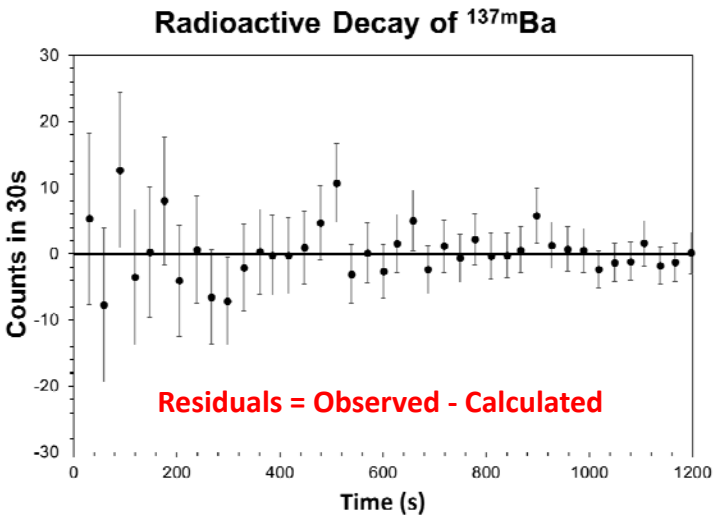
How to Assess a Fit:

#3: Check the Residuals Plot



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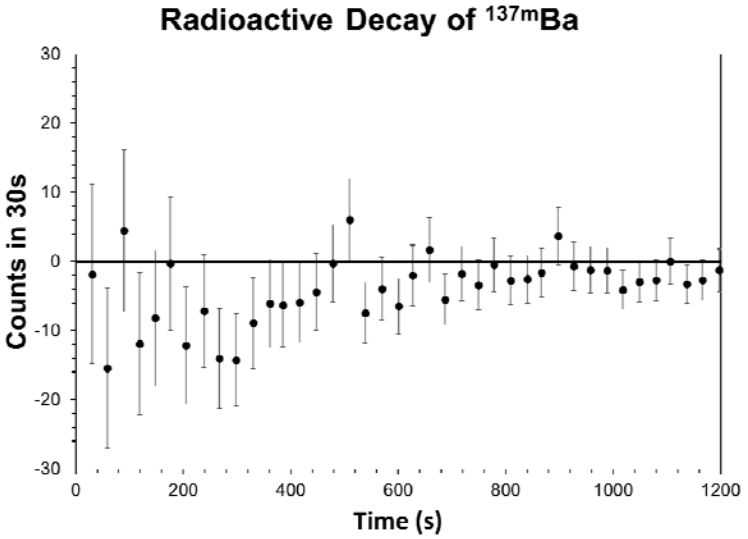
Bad Fit Example:

Model Over-Predicts Data



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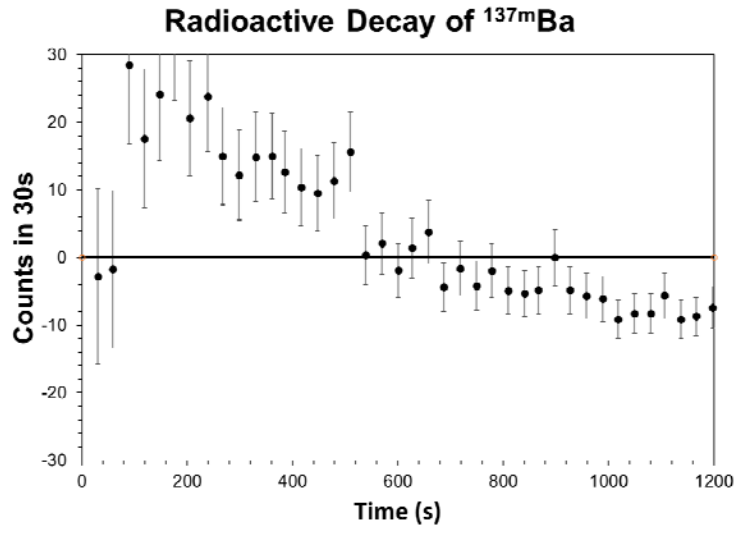
Bad Fit Example:

Systematic Trends in Residuals



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Biochemical Model Building

- **Step 1:** Come up with a hypothesis about how a system works
  - How many binding sites?
  - Is there cooperativity?
- **Step 2:** Translate the qualitative hypotheses into an observable mathematical form with *parameters*
  - Example parameters: K, tau, N
  - Parameters may not be known
- **Step 3:** Design an experiment that that can produce observables from step 2; perform the experiment
  - *Optimize* the parameters to make the fit look as good as possible
- **Step 4:** Assess the fit – Is the agreement convincing?

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Summary

- Biochemical models allow us to quantify and predict the behavior of biological systems
- Fitting parameters allow us to optimize agreement between model and observations
- Programs like Gnuplot enable generalized model fitting with statistical analysis